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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	6

DATE MAILED: 02/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary	Application No.	Applicant(s)	
	08/436,892	PETERSON, THOMAS D.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *09 January 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7,8,11-14 and 16-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4/5* .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, 9-10, and 15, drawn to a method for determining whether a drug qualifies as an LDL-clearance enhancing drug by assessing its capacity to change the three dimensional conformation of apolipoprotein B-100, classified in class 435, subclass 7.92, for example.

II. Claims 7-8, 11-14, and 16-20, drawn to a method to determine whether an elevated cholesterol level is from genetic alteration of apolipoprotein B-100, classified in class 424, subclass 9.2, for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different operation, different functions and different effects in that Invention I requires addition of a compound to cause a change in the three dimensional conformation of apolipoprotein B-100 and quantitating the concentration of a complex formed and Invention II involves diagnosing and treating a genetic alteration condition in a host requiring administering an effective amount of a compound to the host.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper. Literature search for each method and apparatus is distinct since the structural requirements of each invention are different. While searches would be expected to overlap, there is no reason to expect the searches to be coextensive.

During a telephone conversation with Charles Vorndran on 1/9/01 a provisional election was made, with traverse, to prosecute the invention of Group I, claims 1-6, 9-10, and 15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7-8, 11-14, and 16-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Accordingly, claims 1-6, 9-10 and 15 are under examination.

Abstract

2. The abstract of the disclosure is objected to because the content as written is unclear and indecipherable. Correction is required. See MPEP § 608.01(b).

Drawings

3. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings in this application are also objected to by the Draftsperson (see PTO-948 attached). Correction is required. However, formal correction of noted defect can be deferred until application is allowed by the examiner.

Information Disclosure Statement

4. The Information Disclosure Statement (PTO-1449) filed 3/2/00 in Paper No. 4 is acknowledged. References AQ-AV were not considered because neither an English translation nor a statement of relevancy was provided therefor.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-6, 9-10 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in reciting "A method to assess whether a compound is an LDL clearance enhancing drug **that includes** mixing ...; isolating ..., and determining ..." because it is unclear what other method steps should still be included in the claim.

Claim 1 is indefinite in reciting "LDL" and "apoB-100". Acronyms and abbreviations should be recited at least one time in a given set of claims.

Claim 1 is indefinite and confusing in reciting "mixing the drug with cholesterol-containing lipoprotein *in vivo*" because it is unclear, as recited, how this step mechanism is effected.

Claim 1 lacks antecedent support in reciting "isolating **the** complex" in line 3. For example, do Applicants intend that the mixing of the drug with the cholesterol-containing lipoprotein causes a complex formation therebetween. Alternatively, claim 1 is indefinite and confusing in reciting "the binding of the compound to the complex" because it is unclear what elements are encompassed in this second complex. Specifically, it is unclear what structural cooperative relationship exists between "the complex", first occurrence in line 3 and "the complex", second occurrence in line 3 of claim 1.

Claim 1 lacks antecedent support in reciting "**the** LDL receptor" in line 5.

Claim 1 is vague and indefinite in reciting "not probucol or ..., not a compound ..., not a silyl compound ..." because the claim includes elements not actually disclosed (those encompassed by "not probucol and not silyl compound"), thereby rendering the scope of the claims unascertainable.

Regarding claim 1, the phrases "described in WO 98/09773" and "described in US Patent Nos. 5,155,250 or 5,608,095" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "described in ..."), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d). The claim fails to distinctly recite what "compounds" are encompassed within the scope of the instant invention.

Claim 3 is indefinite in reciting "VLDL". Acronyms and abbreviations should be recited at least one time in a given set of claims.

Claim 4 is indefinite in reciting "ELISA". Acronyms and abbreviations should be recited at least one time in a given set of claims.

Claim 4 lacks sufficient clear antecedent support in reciting "binding of the compound to the complex" because it is unclear which "complex" in claim 1, line 3 (first occurrence or second occurrence) is being referred back to for antecedent support. Therefore, it is further unclear what structural cooperative relationship exists between "the complex" in the instant claim and "the complex", first and second occurrence in line 3 of claim 1.

Claim 5 lacks sufficient clear antecedent support in reciting "binding of the compound to the complex". Same analogous problems and comments in claim 4 apply to claim 5.

Claim 6 is indefinite and confusing in reciting "mixing the cholesterol-containing lipoprotein *in vivo* with a compound " because it is unclear, as recited, how this step mechanism is effected.

Claim 6 lacks antecedent support in reciting "**the** complex" in line 3. Specifically, claim 6 is indefinite and confusing in reciting "the binding of the compound to **the** complex" because it is unclear, as recited, what elements are encompassed in the complex.

Claim 9 is indefinite and confusing because the preamble appears to intend a method claim but the limitations thereafter are drawn to "elements" that exclude specific method steps to carry out the method.

Claim 9 is indefinite in reciting "therapeutically useful" because the phrase "therapeutically useful" is a subjective phrase that lacks a comparative basis for defining its metes and bounds.

Claim 9 is vague and indefinite in reciting "directed to an epitope" because it is unclear what is encompassed by the term "directed". For example, is the antibody "specific to" an epitope on the apoB-100.

Claim 9 is indefinite in using parenthetical symbols because it is unclear as to whether limitations within the parenthesis are part of the claim.

Claim 9 is indefinite in reciting "known to be important" because the term "important" is a subjective term that lacks a comparative basis for defining its metes and bounds.

Claim 9 lacks antecedent support in reciting "**the** LDL receptor binding process".

Claim 9 is vague and indefinite in reciting "laid onto a plate" because it is unclear what is encompassed by the term "laid". For example, is the antibody "immobilized, covalently attached" onto a plate.

Claim 9 is indefinite, confusing, and uses inconsistent language in reciting "the cholesterol-containing lipoprotein/test compound complex" and "LDL complex". Alternatively, it is unclear what structural cooperative relationship exists between the two aforementioned recited complexes.

Claim 9 fails to recite a positive limitation or statement in reciting "which can be polyclonal or monoclonal".

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: "mixing/binding/complexing the test compound with the cholesterol-containing lipoprotein" prior to the assessment step.

Claim 15 lacks antecedent support in reciting "isolating **the** resulting complex" in line 3. For example, do Applicants intend that the mixing of the drug with the cholesterol-containing lipoprotein causes a complex formation therebetween. Alternatively, claim 15 is indefinite and confusing in reciting "the binding of the compound to the complex" because it is unclear what elements are encompassed in the complex in line 4. Specifically, it is unclear what structural cooperative relationship exists between "the complex", in line 3 and "the complex", in line 4 of claim 15.

Claim 15 lacks antecedent support in reciting "**the** LDL receptor" in line 5.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1-3, 6, and 15 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by MAO et al. (WO 95/15760).

MAO et al. disclose a method for assessing whether a compound binds to a lipoprotein in a manner which lowers plasma cholesterol by administering or mixing the compound/drug with a cholesterol-containing lipoprotein in vivo, incubating the resulting complex, and determining whether the binding of the compound to low density lipoprotein (LDL) causes a change in the conformation of apoB-100 in the lipoprotein thus enhancing its affinity to LDL receptor (see Abstract and page 2). Specifically, MAO et al. disclose administering certain 2,6-di-alkyl-4-silyl-phenols including those synthesized in pages 7-14 to lower cholesterol levels in patients with hypercholesterolemia. The compound can be administered orally, subcutaneously, intramuscularly, intravenously, etc. (see page 16).

7. Claims 1-3, 6, and 15 are rejected under 35 U.S.C. 102(b) as being inherently anticipated by OATES et al. (The New England Journal of Medicine, 1988).

Oates et al. teach a compound/drug (mevastatin or compactin and lovastatin) that inhibits HMG-CoA reductase and markedly lowers cholesterol and LDL levels in patients. Oates teach that in assessment studies, reductase inhibitors are administered to patients and found that they appear to increase receptor mediated clearance of LDL in the patients; thus qualifying as LDL clearance enhancing drugs (see page 25).

8. Claims 1-5 and 9-10 are rejected under 35 U.S.C. 102(e) as being anticipated by KOREN et al. (US 6,107,045).

Koren et al. disclose quantifying immunoreactive concentrations of lipoprotein and apolipoprotein (LDL and VLDL) using sandwich immunoreactivity assays wherein antibodies specific to apoB-100 (known to be important in LDL receptor binding process) are immobilized into microwells as capture antibodies and labeled as secondary antibodies to capture and quantify the LDL concentration, respectively (see columns 11-12). Immunoreactive concentration of LDL is determined by ELISA or polyacrylamide gel electrophoresis (see columns 13, 18, and 20).

9. No claims are allowed.

Remarks

10. Prior art made of record are not relied upon but considered pertinent to the applicants' disclosure:

BUCALA et al. (WO 94/20083) disclose that the oxidation of lipid component of LDL results in the loss of recognition of the apoB component by cellular LDL receptors (see page 2). Accordingly, Bucala et al. disclose a therapeutic strategy for the treatment of atherosclerosis in which LDL levels are elevated comprising administration of an agent capable of neutralizing the activity of reactive aldehyde products of in vivo lipid oxidation (see page 9).

HEARTLEIN et al. (US 6,027,921) disclose a method to assess whether a compound is an LDL clearance enhancing drug (pharmaceutical composition) by administering the drug to a patient and then determining whether the binding of the drug to LDL causes a change in the conformational state of apoB-100 in the LDL; thereby enhancing its transport into liver cells, regardless of the number or functionality of LDL receptors (see column 8). Specifically, the drug contains a chimeric protein which binds LDL and a cell surface receptor (not the LDL receptor) to form LDL-chimeric protein complexes then transported into cell (see column 4, lines 7-32).

BOGER et al. (5,939,424) disclose a compound for treating disorders of lipid metabolism. Boger et al. provides 4-amino-2-ureidopyrimidine-5-carboxamide compounds which have low toxicity levels. These pharmaceutical compounds effectively stimulate functionality of LDL receptors; thereby, lowering plasma lipid levels (see column 1 and 8).

FRISHMAN et al. (J. Clin. Pharmacol., 1989) teach lovastatin and other HMG-CoA Reductase inhibitors.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
January 27, 2001
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

01/29/01